

Dedicated to the 110th anniversary of M.I. Kabachnik's birth

The Kabachnik–Fields Reaction in the Synthesis of Polyaminophosphonate Derivatives of *p*-*tert*-Butylthiacalix[4]arene

K. S. Shibaeva^a, O. A. Mostovaya^a, A. A. Nazarova^a, D. N. Shurpik^a,
I. E. Shiabiev^a, D. I. Kuznetsova^a, and I. I. Stoykov^{a*}

^a Kazan Federal University, Butlerov Chemistry Institute, ul. Kremlevskaya 18, Kazan, Tatarstan, 420008 Russia

*e-mail: ivan.stoikov@mail.ru

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Abstract—Novel derivatives of *p*-*tert*-butylthiacalix[4]arene containing four or eight 1-aminophosphonate groups at the lower rim of the macrocycle in 1,3-*alternate* conformation have been synthesized via the Kabachnik–Fields reaction. These compounds are promising synthetic receptors for biologically important acids. It has been shown that complete phosphorylation of the first generation dendrimer containing eight primary amino groups is impeded in the case of cyclic ketones.

Keywords: Kabachnik–Fields reaction, thiacalix[4]arene, aminophosphonate

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Creation of synthetic receptors which can molecularly recognize biologically important objects such as dicarboxylic, α -hydroxy, and α -amino acids is a prospective direction of organic chemistry due to the possible applications as models of enzymes, biochemical sensors, and other uses which are significantly important for control of drugs quality, analysis of food, and medical diagnostics [1, 2]. Various (macro)cyclic structures (crown ethers [3, 4], cucurbiturils [5], calixarenes [4–8], pillararenes [9–11]) have been recognized as the most successful molecular platforms for synthesis of such receptors.

The combination of proton-acceptor phosphoryl and proton-donor amino groups allows tuning of the complexing properties of these compounds [12]. The location of the binding sites on a macrocyclic platform significant enhances the complexation selectivity [12–14]. For example, E. Dalcanale's group has recently reported on highly selective receptors for *N*-methylated amino acids based on tetraphosphonate derivatives of resorcinarenes [15]. Furthermore, we have earlier obtained derivatives of *p*-*tert*-butylthiacalix[4]arene **1** and **2** containing one or four 1-aminophosphonate units at the lower rim and shown that the prepared

p-*tert*-butylthiacalix[4]arene **2** containing four α -amino - phosphonate fragments is capable of selective extraction of aspartic acid from the mixture of dicarboxylic, α -hydroxy, and α -amino acids [16]. High selectivity of the acid extraction achieved only in the case of tetra-substituted product is due to spatial complementarity of the coordination site of the thiacalixarene and the *guest* structure [16]. Hence, the preparation of selective synthetic receptors based on thiacalixarene [17] for recognition of carboxylic, α -hydroxy, and α -amino acids is an important issue, resolution of which can lead to the creation of efficient biosensor systems (Scheme 1).

Obviously, the number of aminophosphonate units in the molecule as well as the nature of lipophilic moiety at the α -carbon atom may affect the complexing ability of such synthetic receptors [12]. In view of this, we herein report the synthesis of novel derivatives of *p*-*tert*-butylthiacalix[4]arene containing four or eight 1-aminophosphonate units at the lower rim of the macrocycle with different substituents at the α -carbon atom. It should be noted that the size of dendrimers in the case of octakis(1-aminophosphonate) derivatives is close to 1 nm [18]; this fact opens new possibilities to create biomimetic supramolecular systems [19].